

Scientific Abstract

Angiosarcomas are rare soft tissue sarcomas; malignant angioendothelioma is a unique form of angiosarcoma which develops on the face and scalp of usually older people and carries a relatively poorer prognosis than other forms of sarcoma. In the common presentation of angiosarcoma, extensive local growth is common and margins are difficult to define surgically. The poor prognosis may reflect the fact that clinical diagnosis is often delayed until the disease is advanced. Metastasis to regional lymph nodes and to the lungs occurs, often after repeated surgical excision of the primary growth. The presence of metastatic disease suggests that a therapeutic approach aimed at inducing both a local and a systemic anti-tumor immune response may be beneficial for these patients.

Administration of agents that modulate the immune system may be effective in restoring an immune response against the tumor. Interferon-alpha (IFN- α) is one agent known to modulate the immune system. IFN- α is known to have antiviral, antiproliferative, immunoregulatory, and antiangiogenic properties. The recombinant protein has been approved for use in many clinical indications, including hairy cell leukemia, chronic hepatitis B and C, Kaposi's sarcoma, and chronic myelogenous leukemia. The recombinant protein has been approved for use in many clinical indications, including hairy cell leukemia, chronic hepatitis B and C, Kaposi's sarcoma, and chronic myelogenous leukemia.

In animal models, the partial or complete regression of several types of tumors has been observed following direct intratumoral administration of IFN- α Gene Medicine, a non-viral gene therapy consisting of a plasmid which expresses human interferon-alpha 2b formulated with the synthetic polymer polyvinylpyrrolidone in saline. When administered intratumorally to tumor-bearing mice, IFN- α Gene Medicine leads to a decrease in the rate of tumor progression, with complete tumor regression in some cases. In cases where tumor rejection occurs, the animals also demonstrate immunity to re-challenge with the same tumor cell type. These data suggest that administration of the IFN- α Gene Medicine leads to the generation of an anti-tumor immune response. It is anticipated that the anti-tumor immune response will promote tumor regression, inhibition of tumor progression, and/or prevention of metastasis in humans.

The clinical studies proposed are directed at expressing human IFN- α at a tumor site by non-viral, polymer-mediated delivery of a gene encoding IFN- α . This gene transfer is intended to induce expression of IFN- α in or around the tumor at levels sufficient to promote an anti-tumor response without high concentrations of IFN- α protein in the bloodstream. In animal experiments conducted to address this particular safety issue, a concentration of IFN- α plasmid DNA sufficient to bring about an anti-tumor response did not lead to significant systemic levels of the protein. In addition, preclinical toxicology testing in nonhuman primates demonstrated the absence of side effects of IFN- α Gene Medicine through the highest dose tested, 12 mg/kg. To date, IFN- α Gene Medicine has been administered by direct intratumoral injection in patients with squamous cell carcinoma of the head and neck; doses of IFN- α Gene Medicine have ranged from 3-6 mg per injection and there have been no drug-related side-effects. Thus, IFN- α Gene Medicine may provide clinical anti-tumor efficacy without the side effects observed after high dose systemic administration of recombinant Interferon alpha protein.